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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/948,393	10/10/1997	DENISA D. WAGNER	CFBF-P02-002	6939

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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/21/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/948,393	WAGNER ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on 5/5/04; 8/3/04

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _____ is/are pending in the application. 71-73, 77-81, 83-95

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _____ is/are rejected. 71-73, 77-81, 83-95

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.

5)☐ Notice of Informal Patent Application (PTO-152)

6)☐ Other: _____.

DETAILED ACTION

1. Applicant's Brief on Appeal, filed 8/3/04, is acknowledged.

Applicant's After Final Amendment, filed 5/5/04, has not been entered.

Applicant's amendment to recite "synthetic analogs" raised new issue and consideration and did not place the application in better form for appeal.

Further, applicant is reminded that the instant claims have been under consideration as they read on the elected invention, drawn to methods of treating or inhibiting atherosclerosis with PSGL-1, fragments and chimeric constructs thereof and not synthetic analogs or mimetics of PSGL-1.

The examiner apologizes for any inconvenience in this matter.

Upon reconsideration, New Grounds of Rejection have been set forth to address the claim limitation restenosis.

2. Claims 71-73, 77-81 and 83-95 are pending.

Claims 1-70, 74-76, 82 have been canceled previously.

Claims 71-73, 77-81 and 83-95 are under consideration as they read on the elected invention, drawn to methods of treating or inhibiting atherosclerosis with PSGL-1, fragments and chimeric constructs thereof.

As pointed our previously, the following of record has been noted.
For examination purposes, the use of PSGL-1, fragments and chimeric constructs thereof have the inherent property of inhibiting E-selectin-mediated interactions. If applicant disagrees with this assessment, then such claims would be removed from consideration as they on the elected invention. Also, analogs of PSGL-1 read on fragments and chimeric constructs thereof.
If applicant disagrees with this assessment, then such claims would be removed from consideration as they on the elected invention
For examination purposes, PSGL "on a leukocyte" (e.g. neutrophil, monocyte) reads on PSGL and not on the administration of cells per se.

Claims 71-73, 77-81 and 83-95 as they read on methods of treating or inhibiting atherosclerosis with agents other than PSGL-1 have been withdrawn from consideration by the examiner 37 CFR 1.142(b), as being drawn to a nonelected inventions.

3. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 8/3/04.
The rejections of record can be found in the previous Office Actions.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

Given that applicant has argued that claim 95, drawn to methods for treating "restenosis" stands or falls on its own.

Newly added references have been added to add further evidence to the references of record that the prior art renders such claims drawn to method for treating restenosis in a mammal to which a vessel-corrective technique is administered, encompassed by instant claim 95.

4. Claims 71-73, 77-81 and 83-90 are rejected under 35 U.S.C. § 102(e) as being anticipated by Cummings et al. (U.S. Patent No. 5,464,778) (see entire document) for the reasons set forth in the previous Office Actions and addressed herein.

Claims 71-73, 77-81 and 83-95 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cummings et al. (U.S. patent No. 5,464,778) in view of Larsen et al. (U.S. Patent No. 5,840,679), Tedder et al. (U.S. Patent No. 5,834,425), Coller et al. (U.S. Patent No. 5,976,532) and Sluiter et al. (J. Cardiovascular Pharmacology 22 (Suppl. 4): S37-S44, 1993) for the reasons set forth in the previous Office Actions and addressed herein.

Applicant's arguments in conjunction with the 1.131 declaration under 37 C.F.R. § 1.131, filed 3/18/03 in conjunction with the Appeal Brief, filed 8/3/04, have been fully considered but are not found convincing essentially for the reasons of record.

Applicant's arguments and the examiner's rebuttal are essentially the same of record.

However, the following is noted. In contrast to applicant's assertions that the examiner has conceded to a number of points, including the broad discovery encompassing the specific treatment method described in the pending claims, the following of record is reiterated for applicant's convenience as to what the previous Office Action did address.

Applicant asserts that the original claims encompassed the genus as well as the species and it is only as a result of the restriction requirement imposed by the examiner that applicant was required to limit their claims to selected species. Applicant believes that the possession of the genus is sufficient to constitute possession of the species. Applicant believe that the 131 Declaration is adequate and sufficient to antedate the Cummings et al. Reference since the declaration shows that applicant was in possession of the genus which include the species of Cummings et al.

Applicant asserts that the enclosed Declaration by the co-inventors demonstrates that the conception of the instant invention occurred as early as 1988 and that an actual reduction to practice occurred as early as 9/13/93. The time period between 11/16/92 and 9/13/93 was consumed by the development of a knockout mouse model for atherosclerosis and the testing of the mouse model to verify the inventive concept. It is noted that the conclusion of the results of the experiment were collected and analyzed on or about 5/6/94.

Applicant's rely on the statement: " Macrophages eat bits of activated platelets. ELAM-1 = Padgem. Do monocytes bind to Padgem on platelets. Padgem is an opsonizing agent to get rid of debris of platelets." Applicant assert their conception of a functional relationship between E-selectin and P-selectin, and that P-selectin mediates the binding of platelets to macrophages (leukocytes implicated in atherosclerosis).

Applicant relied upon the preparing a P-selectin knock-out mouse to study the role of P-selectin in atherosclerosis by feeding the P-selectin deficient mice with a lipid diet. The results of this study demonstrate a reduction in the size of atherosclerotic lesions in P-selectin deficient mice.

Applicant assert that based upon these results that inhibitors of P-selectin/ligand binding and/or E-selectin/ligand binding would be useful for the treatment or inhibition of atherosclerosis, constituting an actual reduction to practice the claimed invention.

The evidence, submitted is insufficient to establish a reduction to practice of the invention in this country prior to the effective date of the prior art.

The 37 CFR 1.131 declaration must establish possession of either the whole invention claimed or something falling within the claim in the sense that the claims as a whole reads on it. In re Tanczyn 146 USPQ 298 (CCPA 1965). See MPEP 715.02.

Applicant has not overcome the prior art rejection by showing that the differences between the claimed invention and the showing under 37 CFR 1.131 would have been obvious to one of ordinary skill in the art, in view of applicant's 37 CFR 1.131 evidence, prior to the effective date of the references(s) or the activity.

The test is whether the facts set out in the affidavit are such as would persuade one skilled in the art that the application possessed so much of the invention as is shown in the references. In re Schaub 190 USPQ 324 (CCPA 1976). See MPEP 715.03.

Applicant's evidence of conception and diligence does not address the critical elements of the instant claims which are drawn to a method of treating or inhibiting atherosclerosis in a mammal by administering PSGL-1.

There is insufficient evidence the ordinary artisan would have taken applicant statement: " Macrophages eat bits of activated platelets. ELAM-1 = Padgem. Do monocytes bind to Padgem on platelets. Padgem is an opsonizing agent to get rid of debris of platelets." to establish possession of treating atherosclerosis in a mammal by administering PSGL-1.

Similarly there is insufficient evidence the ordinary artisan would have taken applicant preparation of a P-selectin knock-out mouse to study the role of P-selectin in atherosclerosis by feeding the P-selectin deficient mice with a lipid diet to establish possession of treating atherosclerosis in a mammal by administering PSGL-1.

Further, it is noted that applicant's evidence relies upon experimental animals serves as model systems to selectively investigate different steps of the injury cascade providing specific insights into key mechanisms operating in diseases. While applicant's studies with a P-selectin knockout mouse may have provided insights into the role of P-selectin to atherosclerosis, there is insufficient evidence and correlation of establishing possession of treating atherosclerosis in a mammal by administering PSGL-1, particularly given the absence of any disclosure of administering PSGL-1 in applicant's 131 Declaration and Exhibits.

Also, applicant has not provided objective evidence that applicant was in possession of PSGL-1 itself as well as its use as a therapeutic agent in treating atherosclerosis prior to the disclosure of the prior art. Applicant's reliance on a generic concept of a possible role of P-selectin in atherosclerosis and subsequent findings in an experimental animal model does not support the use of PSGL-1 in treating atherosclerosis.

Absent a clear support or facts are establishing applicant's assertions of conception and diligence (and reduction to practice or subsequent reduction to practice) before the prior art, applicant's arguments are not found persuasive and the rejection is maintained for the reasons of record (e.g., see Paper Nos. 44, 46 and 48).

Again it is noted that Cummings et al. teach the use of PSGL in the treatment of leukocyte adherence, inflammation and coagulation, including ischemia-reperfusion injury and atherosclerosis (see column 18, paragraphs 5-8; columns 19-20, overlapping paragraph).

Applicant asserts that Cummings et al. is directed to treating the inflammatory conditions resulting from the rupture of atherosclerotic lesions or plaque occurring which after the disease (atherosclerosis) has progessed to its end stages (see column 19, lines 57-64), which is distinct from the claimed methods directed to preventing the formation or growth of atherosclerotic lesions (i.e. conditions leading to the development of atherosclerosis).

However, the combination of references does provide sufficient motivation and expectation of success in providing chimeric PSGL-1 to treat various disorders and conditions associated with platelet-leukocyte interactions including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, encompassed by the claimed methods. For example, see Clinical Applications on columns 18-22 and Claims of Cummings et al. Cummings et al. also teach that both acute and chronic disorders are targeted therapies (see column 18, paragraph 5) as well as the pathological situations arising from issue damage resulting from leukocytes associated with ischemia and reperfusion as well as clinical cardiology (see columns 18, paragraphs 6-7 to column 19, paragraph 1).

Given the prior art teachings supporting methods of treating artherosclerosis as well as treating patients undergoing vessel-corrective techniques, decreasing the formation or growth of atherosclerotic lesions as well as treating or inhibiting atherosclerosis would have been an expected or intrinsic property of treating patients undergoing vessel-corrective techniques with PSGL-1.

Coller et al. teach the art known vessel-corrective techniques at the time the invention was made in the treatment of cardiovascular disorders such as atherosclerosis and reocclusion, including angioplasty, atherectomy and coronary bypass surgery (see Background of the Invention on column 1 and Utility of Platelet-specific Chimeric Immunoglobulin on columns 5-7). In teaching the use of an inhibitor of platelet aggregation and thrombus formation associated with such conditions, Coller et al. teach the art known use of combination therapy with other drugs such as thrombolytic agents and that the amounts administered before, along with or subsequent to treatment will depend on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made (see column 6, paragraphs 2-3). Coller et al. teach that antibodies reactive with platelets, including antibodies that bind GMP-140 (i.e. P-selectin) can be used (see column 3, paragraph 3). Therefore, the prior art does teach targeting P-selectin in the context of vessel-corrective procedures.

In contrast to applicant's assertions, Cummings et al. and Coller et al. are drawn to the same or similar methods of inhibiting platelet-leukocyte / endothelial interactions for various clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury as well as cardiovascular disorders such as atherosclerosis and restenosis, including angioplasty, atherectomy and coronary bypass surgery.

Given the art known practice of combination therapy, as taught by Cummings et al. and Coller et al. as well as the art known practice of vessel-occlusive techniques to treat atherosclerosis and restenosis, as taught by Coller et al., one of ordinary skill in the art would have been motivated to administer the PSGL-1 and fragments thereof, as taught by Cummings et al. in various vessel-occlusive techniques given its properties of inhibiting platelet-leukocyte interactions for various clinical applications, including atherosclerosis and ischemia, myocardial infarction and reperfusion injury, as taught by Cummings et al. with an expectation of success.

Sluiter et al. has been provided to add further evidence that the ordinary artisan would have targeted the inhibition of P-selectin-mediated events in therapeutic strategies of inhibiting leukocyte adhesion receptors to alleviate tissue damage in cardiovascular diseases (see entire document, including Figure 1 and Table 1), including those patients suffering from heart attack, atherosclerosis and coronary restenosis (see Concluding Remarks on page S42).

Given the art known practice of modes of administration and dosing depending on a variety of factors and clinical symptoms known to the ordinary artisan at the time the invention was made, as taught by Coller et al. In cardiovascular diseases, the claimed limitations were met or would have been obvious variants in meeting the needs of the patients in order to achieve a therapeutic effect depending on the symptom at the time the invention was made.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller , 642 F.2d 413, 208 USPQ 871 (CCPA 1981); In re Merck & Co., Inc. , 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Applicant's arguments have not been found persuasive for the reasons of record.

5. Claims 71-73, 77-81 and 83-95 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims 40-41, 45, 49-52, 56, 59-60, 73-74 (or appropriate pending claims) as they read on the use of PSGL-1 to treat atherosclerosis of copending application Serial No. 09/436,076 and
claims 39-88 (or appropriate pending claims)as they read on the use of PSGL-1 to treat atherosclerosis of copending application USSN 09/883,642 for the reasons of record.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same or nearly the same methods of treating atherosclerosis with the same or nearly the same PSGL-1, fragments and chimeric constructs thereof.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant's Brief on Appeal, filed 8/4/04, indicates that applicant is prepared to file a terminal disclaimer in this application to overcome this rejection provided that the application is otherwise considered to be in proper condition for allowance.

6. No claim is allowed

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.
Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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October 18, 2004

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